IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No.: (to be assigned)
BUSH *et al.*	Art Unit: (to be assigned)
Appl. No. (to be assigned) (continuation of Appl. No. 09/560,887)	Examiner: (to be assigned)
Filed: October 10, 2001	Atty. Docket: 0609.4540003/JAG/HLK
For: **Use of Clioquinol for the Therapy of Alzheimer's Disease**	

Preliminary Amendment

Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination, kindly amend the above-captioned application as follows. This Amendment is provided in the following format:

(A) A clean version of each replacement paragraph/section/claim along with clear instructions for entry;

(B) Starting on a separate page, appropriate remarks and arguments. 37 C.F.R. § 1.111 and MPEP 714; and

(C) Starting on a separate page, a marked-up version entitled: "Version with markings to show changes made."

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

Amendment

In the Specification:

At page 1, line 2, before "Background of the Invention" please insert

--Cross-Reference to Related Applications

This application is a continuation of Application No. 09/560,887, filed April 28, 2000, which is a continuation of Application No. 09/224,953, filed on January 4, 1999, now abandoned, which is a continuation of Application No. 09/032,777, filed on March 6, 1998, now abandoned. Each of these applications is herein incorporated by reference.--

In the Claims:

Please amend the claims as follows.

Please substitute the following claims 3-5 for currently pending claims 3-5:

3. (Once amended) The method of claim 1, further comprising administering to said patient Vitamin B12.

4. (Once amended) The method of claim 1, wherein the clioquinol is administered intermittently.

5. (Once amended) The method of claim 1, wherein the clioquinol is administered orally.

Please substitute the following claims 8-11 for currently pending claims 8-11:

8. (Once amended) The method of claim 1, further comprising administering trace metals with or subsequent to the administration of the clioquinol.

9. (Once amended) The method of claim 1, wherein the clioquinol is administered parenterally.

10. (Once amended) The method of claim 1, wherein the clioquinol is administered intradermally.

11. (Once amended) The method of claim 1, wherein the therapy is carried out up to 10 years.

Cancel claim 2 without prejudice or disclaimer.

Add new claims 12-46:

--12. A method of treating a subject having or suspected of having Alzheimer's disease comprising administering to the subject an amount of clioquinol effective to treat Alzheimer's disease.

13. The method according to claim 12, wherein the clioquinol is (a) administered for one to 21 days, followed by (b) a period of one to four weeks during which clioquinol is not administered.

14. A method of treating a subject having or suspected of having Alzheimer's disease comprising administering to the subject an amount of clioquinol effective to increase the solubility of amyloid-beta in the cerebrospinal fluid of said subject.

15. A method of treating a subject having or suspected of having Alzheimer's disease comprising administering to the subject (a) an amount of clioquinol effective to treat or prevent Alzheimer's disease, and (b) an amount of vitamin B_{12}.

16. The method according to claim 15 wherein the amount of vitamin B_{12} is effective to inhibit a detrimental side effect of clioquinol administration.

17. The method according to claim 15 wherein a pharmaceutical composition comprising clioquinol is administered for one to 21 days, followed by a period of one to four weeks during which a pharmaceutical composition comprising vitamin B_{12} is administered and clioquinol is not administered.

18. The method according to claim 15 wherein the clioquinol and vitamin B_{12} are administered sequentially.

19. The method according to claim 15 wherein the clioquinol and vitamin B_{12} are administered substantially simultaneously.

20. The method according to claim 16 wherein a pharmaceutical composition comprising clioquinol is administered for one to 21 days, followed by a period of one to four weeks during which a pharmaceutical composition comprising vitamin B_{12} is administered and clioquinol is not administered.

21. The method according to claim 12, 14 or 15, wherein the subject is human.

22. The method according to claim 12 or 15, wherein the clioquinol is administered in an amount of 5-10 mg/kg body weight one to four times daily.

23. The method according to claim 12, wherein trace metals are administered together with or subsequent to the administration of clioquinol.

24. The method according to claim 12 or 15, wherein the clioquinol is administered intermittently.

25. The method according to claim 12, wherein the clioquinol is administered for up to ten years.

26. The method according to claim 12 or 15, wherein the clioquinol is formulated for oral administration.

27. The method according to claim 12 or 15, wherein the clioquinol is formulated for parenteral or intradermal administration.

28. The method according to claim 12 or 15, wherein the vitamin B_{12} is formulated for intramuscular administration.

29. The method according to claim 12 or 15, wherein the vitamin B_{12} is formulated for oral administration.

30. The method according to claim 15, 16 or 17, wherein the clioquinol and vitamin B_{12} are each purified.

31. A pharmaceutical composition comprising an amount of clioquinol effective to treat Alzheimer's disease, and vitamin B_{12}.

32. The pharmaceutical composition according to claim 31, which further comprises a pharmaceutically acceptable carrier.

33. The pharmaceutical composition according to claim 31, wherein the amount of clioquinol is 5-10 mg/kg body weight.

34. The pharmaceutical composition according to claim 31, wherein the amount of vitamin B_{12} is 7-10 mg/kg bodyweight.

35. The pharmaceutical composition according to claim 31, wherein the amount of vitamin B_{12} is 70-100 μg/kg bodyweight.

36. The pharmaceutical composition according to claim 31, wherein the composition is formulated for parenteral or intradermal administration.

37. The pharmaceutical composition according to claim 31, wherein the composition is formulated for oral administration.

38. The pharmaceutical composition according to claim 31 or 32, wherein the clioquinol and vitamin B_{12} are each purified.

39. A pharmaceutical composition comprising a therapeutically effective amount of clioquinol and vitamin B_{12}.

40. The pharmaceutical composition according to claim 39, which further comprises a pharmaceutically acceptable carrier.

41. The pharmaceutical composition according to claim 39, wherein the amount of clioquinol is 5-10 mg/kg body weight.

42. The pharmaceutical composition according to claim 39, wherein the amount of vitamin B_{12} is 7-10 mg/kg bodyweight.

43. The pharmaceutical composition according to claim 39, wherein the amount of vitamin B_{12} is 70-100 μg/kg bodyweight.

44. The pharmaceutical composition according to claim 39, wherein the composition is formulated for parenteral or intradermal administration.

45. The pharmaceutical composition according to claim 39, wherein the composition is formulated for oral administration.

46. The pharmaceutical composition according to claim 39 or 40, wherein the clioquinol and vitamin B_{12} are each purified.--

Remarks

Prompt and favorable consideration of this Preliminary Amendment is respectfully requested. Claim 2 has been canceled, and claims 12-46 have been added. Upon entry of the foregoing Preliminary Amendment, claims 1 and 3-46 will be subject to examination in the application, with claims 1, 12, 14, 15, 31 and 39 being the independent claims.

Applicants have amended the specification to cross-reference related Application Nos. 09/560,887, 09/224,953 and 09/032,777.

In addition, the application has been amended to add new claims 12-46. These claims were added in the parent application to copy claims from issued U.S. patents. More specifically, new claims 12-27 and 29-30 correspond to claims 1-6, 8-14, 16-19, 22-31 and 38 of U.S. Patent No. 6,001,852, issued on December 14, 1999; and new claims 31-46 correspond to claims 1-9 and 16 of U.S. Patent No. 5,994,323, issued on November 30, 1999; and to claims 21-29 and 36 of U.S. Patent No. 5,980,914, issued on November 9, 1999.

Support for claims 12-46 can be found, *inter alia*, as described in the following table:

Claim	Location of Support in Specification
12	page 1, lines 7-16; page 5, line 21 to page 6, line 20; page 7, lines 24-25; page 18, lines 4-6; page 19, lines 5-6
13	page 3, lines 23-25 and 27-29; page 5, lines 17-20; page 9, lines 3-12.
14	page 6, lines 1-20; page 16, line 14 to page 18, line 6.

Claim	Location of Support in Specification
15	page 3, lines 9-12 and 26-27; page 8, lines 20-26; page 9, lines 1-2 and 11-12; page 19, lines 7-8.
16	page 8, lines 20-26.
17	page 3, lines 23-25 and 27-29; page 5, lines 17-20; page 9, lines 3-12.
18 & 19	page 3, lines 23-25.
20	page 3, lines 23-25 and 27-29; page 5, lines 17-20; page 9, lines 3-12.
21	page 12, line 29 to page 13, line 2; page 18, lines 4-6.
22	page 3, lines 13-15; page 8, lines 6-12, 18-19 and 27-28; page 12, lines 17-19.
23	page 3, lines 11-12 and 22-27; page 19, lines 17-19.
24	page 3, lines 27-29; page 19, lines 17-19.
25	page 4, lines 1-2; page 19, lines 24-25.
26	page 3, lines 26-27; page 10, line 22 to page 11, line 22; page 19, lines 11-12.
27	page 3, lines 26-27; page 12, lines 1-11; page 19, lines 20-22.
28	page 3, lines 16-21; page 19, lines 15-16.
29	page 3, lines 16-21 and 26-27; page 19, lines 13-14.
30	page 11, lines 19-21.
31	page 3, lines 11-12 and 23-25; page 8, lines 23-26; page 9, line 17 to page 12, line 28; page 12, lines 21-23.
32	page 9, lines 17-19; page 10, lines 1-4; page 11, lines 7-14 and 23-26.
33	page 3, lines 13-15; page 8, lines 6-12, 18-19 and 27-28; page 12, lines 17-19.
34	page 3, lines 17-19.
35	page 3, lines 19-21.
36	page 3, lines 26-27; page 12, lines 1-11; page 19, lines 20-21.
37	page 3, lines 16-21 and 26-27; page 10, line 22 to page 11, line 22; page 19, lines 11-12 and 13-14.
38	page 11, lines 19-21.
39	page 3, lines 11-12 and 23-25; page 8, lines 23-26; page 9, line 17 to page 12, line 28; page 12, lines 21-23.
40	page 9, lines 17-19; page 10, lines 1-4; page 11, lines 7-14 and 23-26.
41	page 3, lines 13-15; page 8, lines 6-12, 18-19 and 27-28; page 12, lines 17-19.
42	page 3, lines 17-19.
43	page 3, lines 19-21.

Claim	Location of Support in Specification
44	page 3, lines 26-27; page 12, lines 1-11; page 19, lines 20-22.
45	page 3, lines 16-21 and 26-27; page 10, line 22 to page 11, line 22; page 19, lines 11-14.
46	page 11, lines 19-21.

These changes are believed to introduce no new matter, and their entry is respectfully requested.

Summary

Applicants believe that this application is now in condition for examination. Early notice to this effect is respectfully requested.

Respectfully submitted,

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In the Claims:

The following claims 3-5 have been substituted for currently pending claims 3-5:

3. (Once amended) The method of claim [2] 1, further comprising administering to said patient Vitamin B12 [supplement].

4. (Once amended) The method of claim [2] 1, wherein the clioquinol is administered intermittently.

5. (Once amended) The method of claim [2] 1, wherein the clioquinol is administered orally.

The following claims 8-11 have been substituted for currently pending claims 8-11:

8. (Once amended) The method of claim [2] 1, further comprising administering trace metals with or subsequent to the administration of the clioquinol.

9. (Once amended) The method of claim [2] 1, wherein the clioquinol is administered [parenteraly] parenterally.

10. (Once amended) The method of claim [2] 1, wherein the clioquinol is administered [intradermaly] intradermally.

11. (Once amended) The method of claim [2] 1, wherein the therapy is carried out up to 10 years.

Claim 2 has been canceled.

Claims 12-46 have been added.